ALERT: SOME AIR PURIFIERS AND OZONIZERS USE TITANIUM DIOXIDE (TIO2) WHICH MAY BE CARCINOGENIC (CANCER CAUSING)

There are some popular brands of ozone generators and air purifiers on the market currently being sold that advertise the use of a technology called Activated Oxygen, Plasma, PCO and / or Accelerated Photo-Degradation to remove odours, VOC's, destroy viruses, etc. Some of these use Titanium Dioxide (TiO2), which has recently been suspected of being carcinogenic.

How do you tell if your device uses Titanium Dioxide? Generally, these products produce a very pungent, sharp smell, very much stronger than pure ozone, and it lasts a long time... contact your supplier if you suspect your unit contains TiO2 for confirmation.

NOTE: NO PRODUCTS SOLD BY PROMEDUSA CONTAIN OR USE TITANIUM DIOXIDE (TiO2)

Photocatalytic oxidation (PCO) uses ultraviolet lamps (UV-C) combined with a Titanium Dioxide (TiO_2) catalyst coating that is permanently bonded to a PCO honeycomb panel to oxidize and disinfect volatile organic compound (VOC) gases in the air.

The CDC in current intelligence bulletin #63 has identified Titanium Dioxide (TiO2) as a carcinogenic (cancer causing) substance. The International Agency for Research on Cancer (part of WHO-UN) has also cited Titanium Dioxide (TiO2) and placed it on its hazardous substance list.

The US Occupational Safety and Health Agency (OSHA) and the US National Institute for Occupational Safety and Health (NIOSH), the Canadian Centre for Occupational Health and Safety, and the New Jersey Department of Health have also advised of the potential carcinogenic effects of exposure to Titanium Dioxide.

The appropriate documents are available from our website (www.promedusa.us) for your review and reference.

It is impossible to accurately evaluate the potential harm due to the use of these devices, however it may be prudent to evaluate your employees, colleagues and guests exposure to any possible Titanium Dioxide (TiO2) being emitted from these devices.

Right to Know
Hazardous Substance Fact Sheet

Common Name: **TITANIUM DIOXIDE**

Synonyms: Rutile; Anatase; Brookite

Chemical Name: Titanium Oxide

Date: July 2011 Revision: May 2016

CAS Number:	13463-67-7
Anatase Titanium Dioxide	1317-70-0 (powder form)
Rutile Titanium Dioxide	1317-80-2 (powder form)
RTK Substance Number:	1861
DOT Number:	None

EMERGENCY RESPONDERS >>>> SEE LAST PAGE

Description and Use

Titanium Dioxide is an odorless, white powder. It is used in paints, cosmetics, plastics, paper and food.

Hazard Summary

Hazard Rating	NJDOH	NFPA
HEALTH	2	-
FLAMMABILITY	0	-
REACTIVITY	0	-

CARCINOGEN
POISONOUS GASES ARE PRODUCED IN FIRE.
DOES NOT BURN

Hazard Rating Key: 0=minimal; 1=slight; 2=moderate; 3=serious; 4=severe

- **Titanium Dioxide** can affect you when inhaled.
- **Titanium Dioxide** should be handled as a CARCINOGEN--WITH EXTREME CAUTION.
- Exposure can irritate the eyes, nose and throat.
- **Titanium Dioxide** can irritate the lungs. Repeated exposure may cause bronchitis to develop with coughing, phlegm, and/or shortness of breath.

Reasons for Citation

- **Titanium Dioxide** is on the Right to Know Hazardous Substance List because it is cited by OSHA, ACGIH, NIOSH and IARC.
- This chemical is on the Special Health Hazard Substance List.

SEE GLOSSARY ON PAGE 5.

FIRST AID

Eye Contact
- Immediately flush with large amounts of water for at least 15 minutes, lifting upper and lower lids. Remove contact lenses, if worn, while rinsing.

Skin Contact
- Remove contaminated clothing and wash contaminated skin with soap and water.

Inhalation
- Remove the person from exposure.
- Begin rescue breathing (using universal precautions) if breathing has stopped and CPR if heart action has stopped.
- Transfer promptly to a medical facility.

EMERGENCY NUMBERS

Poison Control: 1-800-222-1222
CHEMTREC: 1-800-424-9300
NJDEP Hotline: 1-877-927-6337
National Response Center: 1-800-424-8802

Workplace Exposure Limits

OSHA: The legal airborne permissible exposure limit (PEL) is **15 mg/m^3** averaged over an 8-hour workshift.

NIOSH: The recommended airborne exposure limit (REL) is **2.4 mg/m^3** for *fine* **Titanium Dioxide**, and **0.3 mg/m^3** for *ultrafine* **Titanium Dioxide**, averaged over a 10-hour workshift.

ACGIH: The threshold limit value (TLV) is **10 mg/m^3** averaged over an 8-hour workshift.

- **Titanium Dioxide** may be a CARCINOGEN in humans. There may be no safe level of exposure to a carcinogen, so all contact should be reduced to the lowest possible level.

Titanium Dioxide Classified as Possibly Carcinogenic to Humans

Titanium dioxide has recently been classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2B carcinogen ''possibly carcinogen to humans''. Titanium dioxide accounts for 70% of the total production volume of pigments worldwide. It is widely used to provide whiteness and opacity to products such as paints, plastics, papers, inks, foods, and toothpastes. It is also used in cosmetic and skin care products, and it is present in almost every sunblock, where it helps protect the skin from ultraviolet light.

With such widespread use of titanium dioxide, it is important to understand that the IARC conclusions are based on very specific evidence. This evidence showed that high concentrations of pigment-grade (powdered) and ultrafine titanium dioxide dust caused respiratory tract cancer in rats exposed by inhalation and intratracheal instillation*. The series of biological events or steps that produce the rat lung cancers (e.g. particle deposition, impaired lung clearance, cell injury, fibrosis, mutations and ultimately cancer) have also been seen in people working in dusty environments. Therefore, the observations of cancer in animals were considered, by IARC, as relevant to people doing jobs with exposures to titanium dioxide dust. For example, titanium dioxide production workers may be exposed to high dust concentrations during packing, milling, site cleaning and maintenance, if there are insufficient dust control measures in place. However, it should be noted that the human studies conducted so far do not suggest an association between occupational exposure to titanium dioxide and an increased risk for cancer.

The Workplace Hazardous Materials Information System (WHMIS) is Canada's hazard communication standard. The WHMIS Controlled Products Regulations require that chemicals, listed in Group 1 or Group 2 in the IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, be classified under WHMIS Class D2A (carcinogenic). The classification decision on titanium dioxide has been published on the IARC website and in a summary article published in The Lancet.

Representatives from Health Canada (National Office of WHMIS) recently consulted with the Quebec CSST and CCOHS (the two main agencies providing WHMIS classifications to the public) regarding the implications of the IARC decision to the WHMIS classification of titanium dioxide. It was agreed that titanium dioxide does now meet the criteria for WHMIS D2A (carcinogen) based on the information released by IARC to date, and that it is not necessary to wait for release of the full monograph.

Manufacturers and suppliers of titanium dioxide are advised to review and update their material safety data sheets and product labels based on this new information as soon as possible. Employers should review their occupational hygiene programs to ensure that exposure to titanium dioxide dust is eliminated or reduced to the minimum possible. Workers should be educated concerning this potential newly recognized risk to their health and trained in proper work procedures.

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

CURRENT INTELLIGENCE BULLETIN 63:

OCCUPATIONAL EXPOSURE TO TITANIUM DIOXIDE (TIO2).

Authors
Dankovic D; Kuempel E; Geraci C; Gilbert S; Rice F; Schulte P; Smith R; Sofge C; Wheeler M; Lentz TJ; Zumwalde R; Maynard A; Attfield M; Pinheiro G; Ruder A; Hubbs A; Ahlers H; Lynch D; Toraason M; Vallyathan V

Source
Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2011-160, (CIB 63), 2011 Apr; :1-119

Link: *https://www.cdc.gov/niosh/docs/2011-160/*

Abstract

In this Current Intelligence Bulletin, the National Institute for Occupational Safety and Health (NIOSH) reviews the animal and human data relevant to assessing the carcinogenicity of titanium dioxide (TiO2) (Chapters 2 and 3), presents a quantitative risk assessment using dose-response data in rats for both cancer (lung tumors) and noncancer (pulmonary inflammation) responses and extrapolation to humans with lung dosimetry modeling (Chapter 4), provides recommended exposure limits (RELs) for fine and ultrafine (including engineered nanoscale) TiO2 (Chapter 5), describes exposure monitoring techniques and exposure control strategies (Chapter 6), and discusses avenues of future research (Chapter 7).

This report only addresses occupational exposures by inhalation, and conclusions derived here should not be inferred to pertain to nonoccupational exposures.

TiO2 (Chemical Abstract Service [CAS] Number 13463-67-7) is a non-combustible, white, crystalline, solid, odorless powder. TiO2 is used extensively in many commercial products, including paints and varnishes, cosmetics, plastics, paper, and food as an anticaking or whitening agent.

TiO2 is produced and used in the workplace in varying particle size fractions including fine (which is defined in this document as all particle sizes collected by respirable particle sampling) and ultrafine (defined as the fraction of respirable particles with a primary particle diameter of <0.1 micron [<100 nm]). Particles <100 nm are also defined as nanoparticles.

The Occupational Safety and Health Administration (OSHA) permissible exposure limit for TiO2 is 15 mg/m3, based on the airborne mass fraction of total TiO2 dust (Chapter 1). ***In 1988, NIOSH recommended that TiO2 be classified as a potential occupational carcinogen and that exposures be controlled as low as feasible [NIOSH 2002].***

This recommendation was based on the observation of lung tumors (non-malignant) in a chronic inhalation study in rats at 250 mg/m3 of fine TiO2 [Lee et al. 1985, 1986a] (Chapter

3). Later, a 2-year inhalation study showed a statistically significant increase in lung cancer in rats exposed to ultrafine TiO2 at an average concentration of 10 mg/m3 [Heinrich et al. 1995]. Two recent epidemiologic studies have not found a relationship between exposure to total or respirable TiO2 and lung cancer [Fryzek et al. 2003; Boffetta et al. 2004], although an elevation in lung cancer mortality was observed among male TiO2 workers in the latter study when compared to the general population (standardized mortality ratio [SMR] 1.23; 95% confidence interval [CI] = 1.10-1.38) (Chapter 2). However, there was no indication of an exposure-response relationship in that study. Non-malignant respiratory disease mortality was not increased significantly (P <0.05) in any of the epidemiologic studies.

In 2006, the International Agency for Research on Cancer (IARC) reviewed TiO2 and concluded that there was sufficient evidence of carcinogenicity in experimental animals and inadequate evidence of carcinogenicity in humans (Group 2B), "possibly carcinogenic to humans" [IARC 2010]. TiO2 and other poorly soluble, low-toxicity (PSLT) particles of fine and ultrafine sizes show a consistent dose-response relationship for adverse pulmonary responses in rats, including persistent pulmonary inflammation and lung tumors, when dose is expressed as particle surface area. The higher mass-based potency of ultrafine TiO2 compared to fine TiO2 is associated with the greater surface area of ultrafine particles for a given mass. The NIOSH RELs for fine and ultrafine TiO2 reflect this mass-based difference in potency (Chapter 5).

NIOSH has reviewed and considered all of the relevant data related to respiratory effects of TiO2. This includes results from animal inhalation studies and epidemiologic studies. NIOSH has concluded that TiO2 is not a direct-acting carcinogen, but acts through a secondary genotoxicity mechanism that is not specific to TiO2 but primarily related to particle size and surface area. The most relevant data for assessing the health risk to workers are results from a chronic animal inhalation study with ultrafine (<100 nm) TiO2 in which a statistically significant increase in adenocarcinomas was observed [Heinrich et al. 1995].

This is supported by a pattern of TiO2 induced responses that include persistent pulmonary inflammation in rats and mice [Everitt et al. 2000; Bermudez et al. 2004] and cancer responses for PSLT particles related to surface area. Therefore, on the basis of the study by Heinrich et al. [1995] and the pattern of pulmonary inflammatory responses,

NIOSH has determined that exposure to ultrafine TiO2 should be considered a potential occupational carcinogen. For fine size (pigment grade) TiO2 (>100 nm), the data on which to assess carcinogenicity are limited. Generally, the epidemiologic studies for fine TiO2 are inconclusive because of inadequate statistical power to determine whether they replicate or refute the animal dose-response data. This is consistent for carcinogens of low potency. The only chronic animal inhalation study [Lee et al. 1985], which demonstrated the development of lung tumors (bronchioalveolar adenomas) in response to inhalation exposure of rats to fine sized TiO2 did so at a dose of 250 mg/m3 but not at 10 or 50 mg/m3. The absence of lung tumor development for fine TiO2 was also reported by Muhle et al. [1991] in rats exposed at 5 mg/m3. However, the responses observed in animal studies exposed to ultrafine and fine TiO2 are consistent with a continuum of biological response to TiO2 that is based on particle surface area. In other words, all the rat tumor response data on inhalation of TiO2 (ultrafine and fine) fit on the same dose-response curve when dose is expressed as total particle surface area in the lungs. However, exposure concentrations greater than 100 mg/m3 are generally not considered acceptable inhalation toxicology practice today.

Consequently, in a weight-of-evidence analysis, NIOSH questions the relevance of the 250 mg/m3 dose for classifying exposure to TiO2 as a carcinogenic hazard to workers and therefore, concludes that there are insufficient data at this time to classify fine TiO2 as a potential occupational carcinogen. Although data are insufficient on the cancer hazard for fine TiO2, the tumor-response data are consistent with that observed for ultrafine TiO2 when converted to a particle surface area metric. Thus to be cautious, NIOSH used all of the animal tumor response data when conducting dose-response modeling and determining separate RELs for ultrafine and fine TiO2. NIOSH also considered the crystal structure as a modifying factor in TiO2 carcinogenicity and inflammation. The evidence for crystal-dependent toxicity is from observed differences in reactive oxygen species (ROS) generated on the surface of TiO2 of different crystal structures (e.g., anatase, rutile, or mixtures) in cell-free systems, with differences in cytotoxicity in in vitro studies [Kawahara et al. 2003; Kakinoki et al. 2004; Behnajady et al. 2008; Jiang et al. 2008, Sayes et al. 2006] and with greater inflammation and cell proliferation at early time points following intratracheal instillation in rats [Warheit et al. 2007]. However, when rats were exposed to TiO2 in subchronic inhalation studies, no difference in pulmonary inflammation response to fine and ultrafine TiO2 particles of different crystal structure (i.e., 99% rutile vs. 80% anatase/20% rutile) was observed once dose was adjusted for particle surface area [Bermudez et al. 2002, 2004]; nor was there a difference in the lung tumor response in the chronic inhalation studies in rats at a given surface area dose of these fine and ultrafine particles (i.e., 99% rutile vs. 80% anatase/20% rutile) [Lee et al. 1985; Heinrich et al. 1995].

Therefore, NIOSH concludes that the scientific evidence supports surface area as the critical metric for occupational inhalation exposure to TiO2. ***NIOSH also evaluated the potential for coatings to modify the toxicity of TiO2, as many industrial processes apply coatings to TiO2 particles. TiO2 toxicity has been shown to increase after coating with various substances [Warheit et al. 2005].*** However, the toxicity of TiO2 has not been shown to be attenuated by application of coatings. NIOSH concluded that the TiO2 risk assessment could be used as a reasonable floor for potential toxicity, with the notion that toxicity may be substantially increased by particle treatment and process modification. These findings are based on the studies in the scientific literature and may not apply to other formulations, surface coatings, or treatments of TiO2 for which data were not available. An extensive review of the risks of coated TiO2 particles is beyond the scope of this document.

NIOSH recommends airborne exposure limits of 2.4 mg/m3 for fine TiO2 and 0.3 mg/m3 for ultrafine (including engineered nanoscale) TiO2, as time-weighted average (TWA) concentrations for up to 10 hr/day during a 40-hour work week. These recommendations represent levels that over a working lifetime are estimated to reduce risks of lung cancer to below 1 in 1,000. The recommendations are based on using chronic inhalation studies in rats to predict lung tumor risks in humans.

In the hazard classification (Chapter 5), NIOSH concludes that the adverse effects of inhaling TiO2 may not be material-specific but appear to be due to a generic effect of PSLT particles in the lungs at sufficiently high exposure. While NIOSH concludes that there is insufficient evidence to classify fine TiO2 as a potential occupational carcinogen, NIOSH is concerned about the potential carcinogenicity of ultrafine and engineered nanoscale TiO2 if workers are exposed at the current mass-based exposure limits for respirable or total mass fractions of TiO2. NIOSH recommends controlling exposures as low as possible, below the RELs. Sampling recommendations based on current methodology are provided

(Chapter 6). Although sufficient data are available to assess the risks of occupational exposure to TiO2, additional research questions have arisen.

There is a need for exposure assessment for workplace exposure to ultrafine TiO2 in facilities producing or using TiO2. Other research needs include evaluation of the (1) exposure-response relationship of TiO2 and other PSLT particles and human health effects, (2) fate of ultrafine particles in the lungs and the associated pulmonary responses, and (3) effectiveness of engineering controls for controlling exposures to fine and ultrafine TiO2. (Research needs are discussed further in Chapter 7).

Keywords
Chemical-composition; Chemical-properties; Chemical-reactions; Chemical-structure; Carcinogenicity; Animal-studies; Humans; Biological-effects; Risk-analysis; Dose-response; Cancer; Lung-cancer; Tumors; Pulmonary-system-disorders; Dosimetry; Exposure-limits; Exposure-assessment; Nanoparticles; Monitoring-systems; Biological-monitoring; Control-methods; Respirable-dust; Particulate-dust; Permissible-limits; Inhalation-studies; Epidemiology; Respiratory-irritants; Adenocarcinomas; Toxicology; Mathematical-models; Crystal-structure; Cytotoxicity; Surface-properties; Coatings; Time-weighted-average-exposure